REMARKS

Amendments to the Claims

The term "an analog of growth hormone releasing factor" was deleted from claim 14. The terms "a) a combination of claim 18; or b)" was deleted from claim 30. Applicants submit that no new matter was introduced by these amendments.

Claim Rejections

The 35 U.S.C. § 112, first paragraph rejections

Claims 1-5 have been rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. Particularly, the Examiner has stated that the specification does not provide reasonable enablement for the use of "growth hormone secretagogues" other than those recited in claims 6-17. The Examiner has also alleged that Applicants have failed to set forth the criteria that define a "growth hormone secretagogue" and have failed to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. The Examiner also has alleged that only a limited number of "growth hormone secretagogue" examples have been set forth and that these examples are neither exhaustive nor define the class of compounds required. Furthermore, the Examiner has asserted that the structural differences among the compounds is great and since the pharmaceutical art is unpredictable that each embodiment must be individually assessed for physiological activity. The Examiner has also stated that one skilled in the art would have to undergo an undue amount of experimentation to make or use the invention commensurate in scope with the claims. Applicants respectfully traverse the 35 U.S.C. § 112, first paragraph rejection of claims 1-5.

Applicants submit that claims 1-5 are fully enabled under 35 U.S.C. § 112, first paragraph, since a person skilled in the art would readily be able to use the "growth hormone secretagogues" in a method for treating systemic lupus erythematosus (hereinafter SLE) as claimed and described in the specification. "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" See *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best

omitted. *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). Also, the scope of the enablement must only bear a "reasonable correlation" to the scope of the claims. *In re Fisher*, 427 F.2d 833, 839 (CCPA 1970).

The USPTO 35 U.S.C. § 112, first paragraph training manual (1996 version) at 8 state that a rejection of claims under 35 U.S.C. § 112, first paragraph it is incumbent upon an Examiner to properly construe the claims before an analysis of enablement can occur. The Examiner must select a definition of the terms used in the claims, based on the Examiner's understanding of what the Applicant intends it to mean, and explicitly set forth the meaning of the term in the Office action. Applicants agree with the Examiner's interpretation that claims 1-5 read on a method of treating SLE using all "growth hormone secretagogues." Applicants respectfully disagree with the Examiner's allegation that Applicants have failed to set forth criteria that define a "growth hormone secretagogue." Contrary to the Examiner's allegation, Applicants have provided criteria that define a "growth hormone secretagogue" at page 24, lines 18-21 and pages 33, line 16 through page 34, line 8 of the specification. Representative embodiments of the "growth hormone secretagogues" have also been provided from page 25 through page 30 of the specification. Applicants submit that one skilled in the art would not have to undergo "undue" experimentation to make the "growth hormone secretagogues" since the preparation of these compounds is known in the art and disclosed in the references cited in the specification. Applicants further submit that one skilled in the art is fully enabled to use "growth hormone secretagogues" according to the methods disclosed in the specification, particularly as described at page 34, line 9 through page 37, line 14 of the specification. The examples do not have to be exhaustive nor do they have to define the class of compounds. The term "growth hormone secretagogue" as used in this invention defines the compounds to be used. The examples applicants have provided are just that-examples.

To sustain a rejection based on failure of the specification to enable how to use, the Examiner must proffer evidence that, when taken together with the nature of the invention as set forth in the specification, would "afford one skilled in the art [to have] basis to reasonably doubt applicants' asserted utility on its face." *In re Brana et al.* 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). The burden of showing that the growth hormone secretagogues can not be used to treat SLE as taught in the specification is on the Examiner. Applicant submits that the utility and supporting disclosure provided by the applicant for the growth hormone secretagogues of the present invention is presumptively valid and therefore is sufficient to establish utility of the growth hormone secretagogues as claimed. Applicants have clearly defined "growth hormone secretagogues" in the specification and have clearly taught how the "growth hormone secretagogues" are used to treat SLE. Applicants also submit that the scope of the enablement

provided to make and use the growth hormone secretagogues to treat SLE bears a reasonable correlation to the scope of the claims. For these reasons applicants respectfully request that the Examiner reconsider and withdraw this rejection of claims 1-5 under 35 U.S.C. § 112, first paragraph.

Claim 14 has been rejected under 35 U.S.C. § 112, first paragraph as containing subject matter that was allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. Particularly, the Examiner has stated that the specification does not provide reasonable enablement for the use of an "analog of a growth hormone releasing factor". With the present amendment of claim 14 the term "analog of a growth hormone releasing factor" has been deleted from that claim, thereby rendering the rejection moot. Since claim 14, as amended, no longer recites the term "analog of a growth hormone releasing factor" applicants respectfully request the Examiner to reconsider and withdraw the 35 U.S.C. § 112, first paragraph rejection of that claim.

The 35 U.S.C. § 112, second paragraph rejections

The Examiner has rejected claims 1-5 and 14 under 35 U.S.C. § 112, second paragraph for allegedly failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

The Examiner has alleged that the term "growth hormone secretagogue" as recited in claims 1-5 renders those claims indefinite as one of ordinary skill in the art would not understand what compounds would or would not be growth hormone secretagogues. Applicants respectfully traverse this rejection of claims 1-5.

Applicants respectfully disagree with the Examiner's allegation that Applicants have failed to set forth criteria that define a "growth hormone secretagogue." Initially, applicants submit that the term "growth hormone secretagogue" is well known in the art.Contrary to the Examiner's allegation, Applicants have provided criteria that define a "growth hormone secretagogue" at page 24, lines 18-21 and pages 33, line 16 through page 34, line 8 of the specification. Representative embodiments of the "growth hormone secretagogues" have also been provided from page 25 through page 30 of the specification. One skilled in the art, in view of the present specification, would clearly understand that a "growth hormone secretagogue" is "a compound that, when administered to a patient, increases the production and/or secretion of growth hormone when compared with baseline plasma concentrations of growth hormone." See specification at page 33, lines 16-18. Furthermore, methodology for identification of

compounds as "growth hormone secretagogues", such as the assay described by Smith et al., in Science, 260, 1640-1643 (1993) are well known in the art and described in the specification from page 33, line 24 through page 34, line 15. Applicants respectfully submit that the definition of "growth hormone secretagogue" is clear and definite to one skilled in the art in view of the present specification. Therefore, applicants respectfully request that the Examiner reconsider and withdraw the 35 U.S.C. § 112, second paragraph rejection of claims 1-5.

The Examiner has alleged that the term "an analog of growth hormone releasing factor" as recited in claim 14 renders that claim indefinite as one of ordinary skill in the art would not understand what compounds would or would not be encompassed by that claim. With the present amendment, the term "an analog of growth hormone releasing factor" has been deleted from claim 14. Therefore the present rejection of claim 14 is moot. For this reason, applicants respectfully request that the Examiner reconsider claim 14, as amended, and withdraw the 35 U.S.C. § 112, second paragraph rejection of that claim.

The 35 U.S.C. § 103(a) rejections

The Examiner has rejected claims 1-7, 10, 14-17 and 30 under 35 U.S.C. § 103(a) for allegedly being obvious over Carpino '369 (WO97/24369) and Carpino '306 (U.S. Patent 6,107,306) in view of Hahn (Chapter 284: "Systemic Lupus Erythematosus" in Harrison's Principles of Internal Medicine, 13th Ed., 1994, 1643-1648. Specifically, the Examiner has alleged that it would have been obvious for one of ordinary skill in the art to employ the elected compound for the treatment of SLE over the combination of Carpino '369 and '306 and Hahn because the selected compound is useful to treat the clinical manifestation of SLE such as peripheral neuropathy and renal involvement.Applicants respectfully traverse the 35 U.S.C. § 103(a) rejection of claims 1-7, 10, 14-17 and 30.

The Federal Circuit has held that "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." *In re Geiger*, 815 F.2d at 688, 2 U.S.P.Q.2d at 1278. The Federal Circuit has also held that "it is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art." *In re Wesslau*, 353 F.2d at 241, 147 U.S.P.Q. at 393. Applicants submit that present claims 1-7, 10, 14-17 and 30 are non-obvious in view of the proper combination of the Carpino and Hahn references.

Applicants agree with the Examiner's statement that the Carpino and Hahn references do not expressly teach the use of the elected compound for treating SLE.

Applicants further submit that the Carpino and Hahn references also do not expressly teach or suggest the use of *any* growth hormone secretagogue for the treatment of SLE. Applicants agree with the Examiner that Carpino '369 and '306 disclose that the growth hormone secretagogues disclosed therein are useful for improving muscle strength and mobility as well as renal homeostasis and for treating osteoporosis, improving bone remodeling, promoting cartilage formation and treating peripheral neuropathy among numerous other indications. With respect to the Hahn reference Applicants agree that the clinical manifestation of SLE can be varied. Applicants note that arthralgias, necrosis of bone, peripheral neuropathy and renal involvement are listed along with *over 50 other clinical manifestations* of SLE in Table 284-2 of the Hahn reference. Applicants also note that Table 284-2 indicates that only certain percentages of patients with SLE present with certain clinical manifestations and that a patient with SLE may not have any arthralgias, necrosis of bone, peripheral neuropathy or renal involvement. Not all patients with SLE suffer from all the symptoms and some patients with SLE may exhibit none of the symptoms in the Carpino '369 and '306 references.

Applicants submit that treatment of a specific symptom of a disease is not necessarily equivalent to the treatment of the disease itself. For example, and by analogy, treatment of a headache caused by hypertension does not equate to treatment of the hypertension itself. Likewise, the disclosure of Carpino '369 and '306 that the growth hormone secretagogues are useful for improving muscle strength and mobility as well as renal homeostasis and for treating osteoporosis, improving bone remodeling, promoting cartilage formation and treating peripheral neuropathy does not equate to the present treatment of SLE. Applicants submit that the Carpino references do not suggest or teach treating a patient suffering from SLE as in any of present claims 1-7, 10, 14-17 and 30. In addition, Applicants submit that Hahn at pages 1647-1648 teaches the use of NSAIDs, antimalarials, calcitonin, bisphosphonates, glucocorticoids, cytotoxic agents and psychoactive drugs in the treatment of SLE. Nowhere does Hahn teach or suggest growth hormone secretagogue therapy. Applicants also submit that Hahn at page 1648 discloses plasmapheresis accompanied by iv cyclophosphamide, cyclosporine, iv gamma globulin, lymph node irradiation, fish oil and antibodies to T lymphocytes as experimental therapies for the treatment of SLE. Applicants note that even among the experimental therapies disclosed by Hahn there is no suggestion of the use of growth hormone secretagogues for treating SLE.

At the time of the present invention one of ordinary skill in the art in possession of Carpino '369 and '306 in view of Hahn would not have found the present invention obvious. The Carpino references do not teach or suggest the treatment of a patient suffering from

SLE with a growth hormone secretagogue as described above. Likewise, the Hahn reference does not suggest the use of growth hormone secretagogues as a therapy or even as an experimental therapy for the treatment of SLE. The Carpino and Hahn references when taken together in their entirety simply do not suggest the present invention. According to the Hahn reference it is entirely possible that a patient suffering from SLE would not have any of the clinical manifestations that the Examiner has cited (i.e. the likelihood of a patient exhibiting peripheral neuropathy is 15% or renal involvement is 5-50%) even after selecting these particular clinical manifestations from the 50 or more manifestations listed. Based on the selection of clinical manifestations required from Hahn and the likelihood that a patient may not exhibit those particular manifestations applicants submit that prior to this invention a person of ordinary skill in the art would not have been motivated to use a growth hormone secretagogue in the treatment of SLE. Applicants submit that proper combination of Carpino '369 and '306 and Hahn therefore does not render claims 1-7, 10, 14-17 and 30 obvious.

Likewise, since the use of growth hormone secretagogues for the treatment of SLE was not known or suggested prior to this invention, applicants submit that the combination therapy of growth hormone secretagogues and a second active compound such as an antimalarial or a glucocorticoid was also not known or suggested prior to this invention for the reasons stated hereinabove. For these reasons Applicants respectfully request the Examiner to reconsider and withdraw the 35 U.S.C. § 103(a) rejections of claims 1-7, 10, 14-17 and 30.

Reinstatement of Claims 8-9, 11-13

Applicants respectfully request reinstatement of claims 8-9 and 11-13 at this time. Applicants submit that claim 11 was previously improperly withdrawn since claim 11 is dependent on claim 10, which is currently being examined. Applicants submit that claims 8-9 and 12-13 are in condition for allowance and should be rejoined as they depend from linking claim 7 which applicants believe is also in condition for allowance.

Conclusion

Applicant, having addressed all points and concerns raised by the Examiner, believes that the application is in condition for allowance and respectfully requests an early and favorable action in light of the foregoing amendment and remarks.

Respectfully submitted,

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